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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/134,333	08/14/1998	SHIRLEY LONGACRE-ANDRE	0660-0135-0X	7863

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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 10/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/134,333	LONGACRE-ANDRE ET AL.	
	Examiner	Art Unit	
	James L. Grun	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2006 and 31 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *134,139-143,145,148-155 and 157-176* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *134,139-143,145,148-155 and 157-176* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 31 July 2006, requesting entry of the response filed 16 June 2006, is acknowledged and has been entered. Claim 176 is newly added. Claims 134, 139-143, 145, 148-155, and 157-176 remain in the case.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 153, 159, 162, 165, 169, 172, and 175 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Longacre (Mol. Biochem. Parasitol. 74: 105-111, 1995) in view of Longacre et al. (Mol. Biochem. Parasitol. 64:191, 1994) for reasons of record.

Claims 134, 139-141, 143, 145, 148-150, and 176 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Longacre in view of Longacre et al., and further in view of Holder et al. (US 5,720,959) for reasons of record in the prior rejection of the similar subject matter of claims 134, 139-141, 143, 145, and 148-150.

Applicant's arguments and the declaration of Shirley Longacre, entered 31 July 2006, have been fully considered but they are not deemed to be persuasive.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re*

Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicant urges that Longacre (1995) fails to teach the use of fragments as claimed in claims 151 and 152. This is not found persuasive because these claims are not rejected under the instant grounds of rejection. Applicant urges that Longacre (1995) merely describes the gene sequence of the *P. cynomolgi* MSP-1 p42. This is not found persuasive because the reference teaches the transfer vector as a step to vaccine trials with fragments of the protein and specifically teaches the use of the transfer vector to make recombinant baculovirus for expression of the *P. cynomolgi* MSP-1 protein fragment comprising the p19 fragment (see e.g. page 109, col. 1). Applicant implies that Longacre fails to teach the use of a fragment having the sequence from amino acid residues 276-380. Notwithstanding applicant's implications to the contrary, the instant use of "consists essentially of" or "comprising" claim language does not exclude a longer recombinant protein, as cloned in Longacre, that contains the relevant fragment as instantly claimed. Applicant has provided no description or evidence that inclusion of other residues of the longer sequence materially changes the character of the composition as both the shorter and longer sequences include the EGF-like domains notoriously well known to the art. Indeed, the recombinant protein expressed in Longacre (1995) contained relevant conformational epitopes of the p19 fragment (again see page 109). Applicant urges that Holder et al. do not teach proteins of malarial parasites infectious for man made recombinantly with a baculovirus. This is not found persuasive in view of Longacre or Longacre et al. Moreover applicant's assertion that Holder et al. teach the sequences of a MSP-1 protein from a murine parasite were not found persuasive because the cited reference (US 5,720,959) teaches *P. falciparum* MSP-1 protein fragments as well as murine fragments. Applicant, in arguments and in the declaration, urges that Longacre or

Longacre et al. do not specifically teach an effective vaccine, particularly one comprising alum. This is not found persuasive for a number of reasons. Firstly, the argument is unpersuasive because a recitation of intended use is accorded patentable weight only to the extent that it limits the actual components of a composition; in the instant case the intended use does not affect the recombinant protein as claimed in any way which distinguishes over the subject matter taught or suggested by the references. Secondly, the argument is also not found persuasive because the missing teaching is clearly provided by the combination of these references with the teachings of Holder et al., discussed at further length *infra*.

Applicant implies that the combined teachings of the references do not suggest the use of a shorter sequence from amino acid residues 276-380, rather than the whole of residues 1-380, and that there is no motivation to combine the teachings of Longacre in view of Longacre et al., and further in view of Holder et al. These are not found persuasive for a number of reasons. Firstly, notwithstanding applicant's assertions to the contrary, for the reasons set forth above incorporated herein, the instant use of "consists essentially of" or "comprising" claim language does not exclude a longer recombinant protein. Secondly, the arguments are not found persuasive because the examiner recognizes that references cannot be arbitrarily combined and that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See: *In re Nomiya*, 184 USPQ 607 (CCPA 1975); *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); or, *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). However, there is no requirement that a motivation to make the modification

be expressly articulated. The test for combining references is what the combination of disclosures taken as a whole would suggest to one of ordinary skill in the art. See: *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re McLaughlin*, 170 USPQ 209 (CCPA 1971). References are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. *In re Bozek*, 163 USPQ 545 (CCPA 1969). In this case, for the reasons of record, ample motivations have been set forth to clone and produce the C-terminal p42 and p19 fragments of MSP-1 proteins as notoriously old and well known vaccine candidates in the art as clearly taught by the references (see e.g. Longacre at al., page 192). Moreover, the examiner would further note the identification of the p42 and p19 cleavage sites in Fig. 1 of Longacre and the teaching in Longacre et al. to include 6 or 7 of the apparently well conserved residues upstream from the cleavage sites in p42 and p19 constructs (see e.g. page 194, col. 2). Such teachings would guide one to residues 276-380 of instant SEQ ID NO: 11, and of the sequence in Longacre, for a *P. cynomolgi* MSP-1 p19 construct. As set forth, Holder et al. teach the incorporation of MSP-1 peptides comprising the EGF domains in vaccine compositions comprising alum.

Applicant, in arguments and in the declaration, urges that the references do not teach a protective response, particularly using alum as adjuvant. This is not found persuasive because the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). As set forth, the C-terminal p42 and p19 fragments of MSP-1 proteins are notoriously old and well known vaccine candidates in the art as clearly taught by the references,

and Holder et al. teach the incorporation of MSP-1 peptides comprising the EGF domains of the p19 fragment in vaccine compositions comprising alum. Applicant's arguments regarding the relative efficacy of various adjuvants were not found persuasive in view of the direct suggestion in the prior art to use alum as adjuvant for an MSP-1 fragment vaccine. Notwithstanding applicant's assertions to the contrary, variable levels of parasitemias in non-inbred hosts were not found persuasive or an unexpected result. Moreover, a recitation of intended use or an intended result is accorded patentable weight only to the extent that it limits the actual components of a composition; in the instant case the intended use does not affect the components in any way which distinguishes over the subject matter taught or suggested by the references. If the prior art composition is capable of performing the intended use, then it meets the claim.

Claims 151, 152, 154, 155, 157, 158, 160, 161, 163, 164, 166, 167, 168, 170, 171, 173, and 174 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combined teachings of Chappel et al (Mol. Biochem. Parasitol. 60:303, 1993), Miller et al (Mol. Biochem. Parasitol. 59:1, 1993), Longacre et al (Mol. Biochem. Parasitol. 64:191, 1994), and Longacre (Mol. Biochem. Parasitol. 74: 105-111, 1995) for reasons of record.

Claims 134, 139-143, 148, 150 and 176 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Chappel et al., Miller et al., Longacre, and Longacre et al., and further in view of Holder et al. (U.S. Pat. No. 5,720,959) for reasons of record in the prior rejection of the similar subject matter of claims 134, 139-143, 148, and 150.

Applicant's arguments and the declaration of Shirley Longacre, entered 31 July 2006, have been fully considered but they are not deemed to be persuasive. Applicant's arguments

regarding the teachings of Longacre, Longacre et al., and Holder et al. have been addressed previously and the examiner's responses are incorporated herein.

Applicant, in arguments and in the declaration, urges that the references do not teach a protective response, particularly using alum as adjuvant. Applicant's arguments have been addressed previously and the examiner's responses are incorporated herein.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Notwithstanding applicant's assertions to the contrary, Chappel et al. is relied upon for the teaching of a recombinant baculovirus producing a soluble *P. falciparum* MSP-1 protein comprising the p19 fragment EGF-like domains, not the fusion proteins as argued. As set forth, Miller et al. teach the sequences of a variety of *P. falciparum* MSP-1 proteins. Notwithstanding applicant's assertions to the contrary, the teaching of two sequences for the first EGF-like domain in Chappel et al. and Miller et al. does not teach away from the use of either sequence, depending upon the range of antigenicity/immunogenicity desired for the suggested composition.

In response to applicant's implications that there are no specific suggestions to combine the references, the examiner recognizes that references cannot be arbitrarily combined and that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See: *In re Nomiya*, 184 USPQ 607 (CCPA 1975); *In re Fine*, 837

F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). However, there is no requirement that a motivation to make the modification be expressly articulated. The test for combining references is what the combination of disclosures taken as a whole would suggest to one of ordinary skill in the art. See: *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re McLaughlin*, 170 USPQ 209 (CCPA 1971). References are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. *In re Bozek*, 163 USPQ 545 (CCPA 1969). In this case, for the reasons of record, ample motivations have been set forth to clone and produce the C-terminal p42 and p19 fragments of MSP-1 proteins comprising the conformational epitopes of the EGF-like domains as notoriously old and well known vaccine candidates in the art as clearly taught by the references (see e.g.: Chappel et al.; Longacre at al., page 192; Holder et al.). As set forth, one would have had a reasonable expectation of the successful use of a plasmid containing the N-terminal signal sequence of *Plasmodium vivax*, containing residues Met_1-Asp_{32} therein, to function in the cloning of a heterologous species MSP-1 fragment in view of its already successful use therefor as taught in Longacre in view of Longacre et al. As set forth, Holder et al. teach the incorporation of MSP-1 peptides comprising the EGF domains in vaccine compositions comprising alum.

Notwithstanding applicant's assertions to the contrary, as notoriously old and well known in the art as taught in the references and as set forth in the rejections of record, one would have expected fragments of various lengths comprising the conformational epitopes of the EGF-like domains to function in a vaccine. Moreover, the examiner would further note the identification of at least the p19 cleavage site in Miller et al. (see e.g. pages 6 and 10) and the teaching in

Longacre et al. to include 6 or 7 of the apparently well conserved residues upstream from the cleavage sites in p42 and p19 constructs (see e.g. page 194, col. 2). Such teachings would guide one to appropriate residues for the *P. falciparum* MSP-1 p19 construct. Further, notwithstanding applicant's assertions to the contrary, the instant use of open claim language does not exclude a longer recombinant protein, as cloned in Chappel et al., that comprises the relevant fragment as instantly claimed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James L. Grun, Ph.D.
September 28, 2006

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